

- (b) a second polynucleotide sequence homologous to a second portion of a ROR $\gamma$  gene; and
  - (c) a selectable marker positioned in between the first and the second polynucleotide sequences.
51. (New) The targeting construct of claim 50, wherein the targeting construct further comprises a screening marker.
52. (New) A method of producing a targeting construct, the method comprising:
- (a) providing a first polynucleotide sequence homologous to a first portion of a ROR $\gamma$  gene;
  - (b) providing a second polynucleotide sequence homologous to a second portion of a ROR $\gamma$ ;
  - (c) providing a selectable marker; and
  - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
53. (New) A method of producing a targeting construct, the method comprising:
- (a) providing a polynucleotide comprising a first sequence homologous to a first region of a ROR $\gamma$  gene and a second sequence homologous to a second region of a ROR $\gamma$  gene;
  - (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.
54. (New) An isolated mouse cell comprising a genome comprising a target gene sequence disrupted by homologous recombination of the target gene sequence with a sequence homologous to a region of SEQ ID NO: 1.
55. (New) The cell of claim 54, wherein the cell is an embryonic stem cell.
56. (New) A transgenic mouse comprising a genome comprising a target gene sequence disrupted by homologous recombination of the target gene sequence with a sequence homologous to a region of SEQ ID NO: 1.
- ~~57. (New) A cell derived from the transgenic mouse of claim 56.~~
58. (New) A method of producing a transgenic mouse comprising a genome comprising a target gene sequence disrupted by homologous recombination of the target gene

sequence with a sequence homologous to a region of SEQ ID NO: 1, the method comprising:

- (a) introducing the targeting construct of claim 50 into a cell;
- (b) introducing the cell into a blastocyst;
- (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
- (d) breeding the chimeric mouse to produce the transgenic mouse.

59. (New) A method of identifying an agent that modulates the expression of a ROR $\gamma$  gene, the method comprising:

- (a) providing the transgenic mouse of claim 56;
- (b) administering an agent to the mouse; and
- (c) determining whether the expression of ROR $\gamma$  in the mouse is modulated.

60. (New) A method of identifying an agent that modulates the expression of a ROR $\gamma$  gene, the method comprising:

- (e) providing the cell of claim 57;
- (f) contacting the cell with an agent; and
- (g) determining whether expression of the ROR $\gamma$  gene is modulated.

61. (New) A method of identifying an agent that modulates the function of a ROR $\gamma$  gene, the method comprising:

- (a) providing the cell of claim 57;
- (b) contacting the cell with an agent; and
- (c) determining whether the function of the ROR $\gamma$  gene is modulated.

62. (New) The transgenic mouse of claim 56, wherein the transgenic mouse exhibits at least one of the following phenotypes: a spleen abnormality, a kidney abnormality, an abnormality of the thymus, an abnormality in the lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones.

63. (New) The transgenic mouse of claim 62, wherein the spleen abnormality is increased-weight of the spleen relative to a wild-type-mouse.

64. (New) The transgenic mouse of claim 62, wherein the spleen abnormality is increased size of the spleen relative to a wild-type mouse.

65. (New) The transgenic mouse of claim 62, wherein the spleen abnormality is an increased spleen to body weight ratio relative to a wild-type mouse.
66. (New) The transgenic mouse of claim 62, wherein the kidney abnormality is increased weight of the kidney relative to a wild-type mouse.
67. (New) The transgenic mouse of claim 62, wherein the kidney abnormality is increased size of the kidney relative to a wild-type mouse.
68. (New) The transgenic mouse of claim 62, wherein the kidney abnormality is an increased kidney to body weight ratio relative to a wild-type mouse.
69. (New) The transgenic mouse of claim 62, wherein the liver abnormality is increased weight of the liver relative to a wild-type mouse.
70. (New) The transgenic mouse of claim 62, wherein the liver abnormality is increased size of the liver relative to a wild-type mouse.
71. (New) The transgenic mouse of claim 62, wherein liver abnormality is an increased liver to body weight ratio relative to a wild-type mouse.
72. (New) The transgenic mouse of claim 62, wherein the thymus abnormality is increased weight of the thymus relative to a wild-type mouse.
73. (New) The transgenic mouse of claim 62, wherein the thymus abnormality is increased size of the thymus relative to a wild-type mouse.
74. (New) The transgenic mouse of claim 62, wherein the thymus abnormality is an increased thymus to body weight ratio relative to a wild-type mouse.
75. (New) The transgenic mouse of claim 62, wherein the abnormality of the thymus is thymic cortical expansion and medullary reduction relative to a wild-type mouse.
76. (New) The transgenic mouse of claim 62, wherein the abnormality of the lymph nodes is depletion of lymph nodes relative to a wild-type mouse.
77. (New) The transgenic mouse of claim 62, wherein the abnormality of the lymph nodes is absence of lymph nodes.
78. (New) The transgenic mouse of claim 62, wherein the abnormality of the lymph nodes is depletion of gut associated lymphoid-tissue ratio relative to a wild-type mouse.

79. (New) The transgenic mouse of claim 62, wherein the abnormality lymphocytes comprises lymphoid infiltrates.
80. (New) The transgenic mouse of claim 62, wherein the abnormality lymphocytes is consistent with lymphoma.
81. (New) The transgenic mouse of claim 80, further comprising at least one of the following symptoms of disease: poor grooming, hypoactivity, increased thoracic girth, and increased abdominal girth, hepatosplenomegaly, enlarged thymus, ascites, weakness, squinting, hunching, cachexis, lethargy, and impaired respiration.
82. (New) The transgenic mouse of claim 62, wherein the bone marrow is pale.
83. (New) The transgenic mouse of claim 62, wherein the abnormality of the bones is brittleness.
84. (New) The transgenic mouse of claim 62, wherein the abnormality of the bones is attached white masses.
85. (New) A method of producing the transgenic mouse of claim 62, the method comprising:
- (a) introducing a ROR $\gamma$  gene targeting construct into a cell;
  - (b) introducing the cell into a blastocyst;
  - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
  - (d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a ROR $\gamma$  gene.
86. (New) A cell derived from the transgenic mouse of claim 62.
87. (New) A cell derived from the transgenic mouse of claim 80.
88. (New) A method of identifying an agent that ameliorates a phenotype associated with a disruption in a ROR $\gamma$  gene, the method comprising:
- (a) administering an agent to a transgenic mouse comprising a disruption in a ROR $\gamma$  gene; and
  - (b) determining whether the agent ameliorates at least one of the following phenotypes: a spleen abnormality, a kidney abnormality a spleen abnormality a liver abnormality, an abnormality of the thymus, an abnormality in the

lymph nodes, an abnormality in the lymphocytes, an abnormality in the bone marrow, or an abnormality in the bones.

89. (New) A method of identifying an agent that ameliorates a phenotype associated with a disruption in a ROR $\gamma$  gene, the method comprising:
- (a) administering an agent to a transgenic mouse comprising a disruption in a ROR $\gamma$  gene; and
  - (b) determining whether the agent ameliorates at least one of the following phenotypes: elevated serum alanine aminotransferase, elevated serum alkaline phosphatases, elevated serum aspartate aminotransferase, elevated blood urea nitrogen, and elevated blood phosphorus.
90. (New) A method of identifying an agent that modulates the expression of a ROR $\gamma$  gene, the method comprising:
- (a) providing the transgenic mouse of claim 62;
  - (b) administering an agent to the transgenic mouse; and
  - (c) determining whether the expression of ROR $\gamma$  gene in the mouse is modulated.
91. (New) A method of identifying an agent that modulates the expression of ROR $\gamma$  gene, the method comprising:
- (a) providing the cell of claim 62;
  - (b) contacting the cell with an agent; and
  - (c) determining whether expression of the ROR $\gamma$  gene is modulated.
92. (New) A method of identifying an agent that modulates the expression of ROR $\gamma$  gene, the method comprising:
- (a) providing the cell of claim 87;
  - (b) contacting the cell with an agent; and
  - (c) determining whether expression of the ROR $\gamma$  gene is modulated.
93. (New) A method of identifying an agent that ameliorates a phenotype associated with a disruption in a ROR $\gamma$  gene, the method comprising:
- (a) administering an agent to the transgenic mouse of claim 81; and
  - (b) determining whether the agent modulates ROR $\gamma$  expression in the transgenic mouse, wherein the agent has an effect on at least one of the following